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Substitu	ute for form 1449	APTO			C mplete if Known	-9	i E	_
		Application Number	09/724,569	-10	٧.	_		
INF	<b>ORMATI</b>	ON DIS	CLOSURE	Filing Date	November 28, 2000	3	()O	
STA	ATEMEN	T BY A	PPLICANT	First Named Inventor	John P. Anderson		9	
		. –		Art Unit	1632	\(\frac{1}{2}\)	55	
(use as many sheets as necessary)		Examiner Name	Unknown		_8_			
Sheet	1	of	6	Attorney Docket Number	015270-006446US			

			U.S. PATENT D	OCUMENTS	
	Cita	Document Number	Publication Date	Name of Patentee or	Pages, Columns, Unes, Where
Examiner	Cite No. <sup>1</sup>	Number Kind Code <sup>2</sup> (if known)	MM-DD-YYYY	Applicant of Cited Document	Relevant Passages or Relevant Figures Appear
il	1	6,361,975	03-26-2002	Christie, et al.	
w	2	6,358,725	03-19-2002	Christie, et al.	RECEIVED
W	3	6,319,489	11-20-2001	Powell, et al.	25011
W	4	6,319,689	11-20-2001	Powell, et al.	DEC 1 1 2002
W.	5	6,313,268	11-06-2001	Hook	TECH CENTER 1600/290
ilWo	6	6,245,884	06-12-2001	Hook	1011 OLIVILI 1000/4900
W	7	6,245,964	06-12-2001	McConlogue, et al.	
ilw -	8	6,221,645	04-24-2001	Chrysler, et al.	
M	9	6,211,428	04-03-2001	Singh, et al.	
tw	10	6,162,630	12-19-2000	Powell, et al.	
W	11	6,025,180	02-15-2000	Powell, et al.	
eW -	12	5,942,400	08-24-1999	Anderson, et al.	
ilw	13	5,877,015	03-02-1999	Hardy, et al.	•
M	14	5,849,560	12-15-1998	Abraham	
dw	15	5,837,672	11-17-1998	Schenk, et al.	
W	16	5,795,963	08-18-1998	Mullan	
ilw	17	5,766,846	06-16-1998	Schlossmacher, et al.	
W	18	5,750,349	05-12-1998	Suzuki, et al.	
ilw	19	5,744,346	04-28-1998	Chrysler, et al.	
W	20	5,733,768	03-31-1998	Dixon, et al.	
W	21	5,593,846	01-14-1997	Schenk, et al.	
W	22	5,455,169	10-03-1995	Mullan	·
w,	23	5,424,205	06-13-1995	Dovey, et al.	
M	112	09/869,414		Gurney, et al.	
M	90	09/794,927		-Gurney, et al:	
W	91	09/794,925		-Gurney, et-al.	

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Examiner Signature	Malicha	Date Considered	12/20/04	

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<sup>&</sup>lt;sup>1</sup> Applicant's unique citation designation number (optional). <sup>2</sup> Kind Codes of U.S. Patent Documents at <a href="https://www.uspto.gov">www.uspto.gov</a> or MPEP 901.04. <sup>3</sup> Enter Office that issued the document, by the two-letter code (WIPO Standard ST.3). <sup>4</sup> For Japanese patent documents, the indication of the year of the reign of the Emperor must precede the serial number of the patent document. <sup>6</sup> Kind of document by the appropriate symbols as indicated on the document under WIPO Standard ST. 16 if possible. <sup>6</sup> Applicant is to place a check mark here if English language Translation is attached.

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Under the Paperwork Reduction Act of 1995, no persons are required to respond to a collection of information unless it contains a valid OMB control number. Substitute for form 1449A/PTO C mplete if Kn wn **Application Number** 09/724.569 INFORMATION DISCLOSURE November 28, 2000 Filing Date STATEMENT BY APPLICANT First Named Inventor John P. Anderson Art Unit 1632 (use as many sheets as necessary) **Examiner Name** Unknown 015270-006446US Sheet Attorney Docket Number

			U.S. PATENT D	OCUMENTS	
Examiner	Cite No. <sup>1</sup>	Document Number  Number Kind Code <sup>2</sup> (if known)	Publication Date MM-DD-YYYY	Name of Patentee or Applicant of Cited Document	Pages, Columns, Lines, Where Relevant Passages or Relevant Figures Appear
W	89	09/795,847	NA NA	Gurney, et al.	
iW	92	09/794,748 /		Gurney, et al.	
ilW	88	09/794,743		-Gurney, et al.	
ilw	111	09/681,442		Gurney, et al.	
W	87	09/551,853		-Gurney, et al.	
ili	96	09\548,376/		Gurney, et al.	
W.	24	09/548,37/3		Gurney, et al.	
W	99	09/548,3/2		Gurney, et al.	
W	94	09/548/370		Gurney, et al.	
MAL	97	09/54/8,3/69		Gurney, et al.	
W.	100	09/5/48,368		Gurney, et al	
iW	98	09/548,367		Gurney, et al.	
W	25	Ø9/548,366 \		Gurney, et al.	
W	95	09/548,365	-	Gurney, et al	
im	26	09/416,901		Gurney, et al.	
W	27	09/404,133		Gurney, et al.	
ill	28	09/277,229		Citron, et al.	
W	29	60/210,292		Hong, et al.	
W.	30	60/178,368		Lin, et al.	
iW	31	60/177,836		Lin, et al.	
iW	32	60/168,060		Lin, et al.	
alw	33	60/155,493		Gurney, et al.	
M	34	60/141,363		Lin, et al.	
illan	35	60/139,172		Anderson, et al.	
ilw	36	60/119,571		Basi, et al.	
w	37	60/114,408	<u> </u>	Basi, et al.	
W	38	60/101,594		Gurney, et al.	

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			FOR	EIGN PATE	NT DOCUMENT	S		
Examiner Initials*	Cite No.1	Country Code	Foreign Patent Documen	t Kind Code <sup>s</sup> (# known)	Publication Date MM-DD-YYYY	Name of Patentee or Applicant of Cited Document	Pages, Columns, Lines, Where Relevant Passages or Relevant Figures Appear	T <sup>0</sup>
M	39	EP	EP 0 855 444	A2	07-29-1998			
iW	40	EP	EP 0 848 062	A2	06-17-1998			
dW.	48	PCT	WO 01/38487	A2	05-31-2001			
W	49	PCT	WO 01/36600	A1	05-25-2001		,	
W	50	PCT	WO 01/31054	A1	05-03-2001			
W.	51	PCT	WO 01/29563	A1	04-26-2001			
W.	52	PCT	WO 01/00665	A2	01-04-2001			
W):	53	PCT	WO 01/00663	A2	01-04-2001			
chy	47	PCT	WO 00/69262	A1	11-23-2000			
JW.	46	PCT	WO 00/68266	A1	11-16-2000			
iW	45	PCT	WO 00/58479	A1	10-05-2000			
iW.	44	PCT	WO 00/56871	A2	09-28-2000	·		
W	43	PCT	WO 00/47618	A3	08-17-2000	. *		
uW	42	PCT	WO 00/23576	A2	04-27-2000			
im	41	PCT	WO 00/17369	A2	03-30-2000			
ilm	54	PCT	WO 99/64587	A1	12-16-1999		_	
W	55	PCT	WO 99/46281	A2	09-16-1999			
um	57	PCT	WO 99/34004	A2	08-07-1999			
ill	59	PCT	WO 99/31236	A2	06-24-1999		•	
UN	60	PCT	WO 98/26059		06-18-1998			
un	61	PCT	WO 98/21589		05-22-1998			
w	62	PCT	WO 98/13488		04-02-1998		-	
Mo	63	PCT	WO 98/11236		03-19-1998			
M	103	PCT	WO 97/47314		12-18-1997			
ild	56	PCT	WO 96/40885	A2	12-19-1996			
MV	58	PCT	WO 96/31122	A1	10-10-1996			
M	102	PCT	WO 96/20725	A2	07-11-1996			
Examiner Signature		Mal	veller		Date Considered	12/20	0/04	

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	Substitute	e for form 1448	B/PTO			Complet_if Known		
					Applicati n Number	09/724,569		
				CLOSURE	Filing Date	November 28, 2000		CEIVED
	STA	TEMEN'	T BY A	PPLICANT	First Named Inventor	John P. Anderson	nE	CEIVED
				,	Art Unit	1632	DF.	C 1 1 2002
		(use as mai	ny sheets as	necessary)	Examiner Name	Unknown		2 1 20,02
	Sheet	4	of	6	Attorney Docket Number	015270-006446US	TEALO	NTER 1600/29
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		OTHER PRIOR ART NON PATENT LITERATURE DOCUMENTS	
Examiner Initials *	Cite No.1	Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc.), date, page(s), volume-issue number(s), publisher, city and/or country where published.	T²
lw	104	Baldwin, et al., Crystal structures of native and inhibited forms of human cathepsin D: Implications for lysosomal targeting and drug design, <i>PNAS USA</i> , 90:6796-6800 (1993).	
lw	105	Brown, et al., Evaluation of Cathepsins D and G and EC 3.4.24.15 as Candidate β-Secretase Proteases Using Peptide and Amyloid Precursor Protein Substrates, Journal of Neurochemistry, 66: 2436-2445 (1996).	
un	106	Chevallier, et al., Cathepsin D displays in vitro $\beta$ -secretase-like specificity, Brain Research, 750:11-19 (1997).	
Lw	64	Chyung, et al. Novel $\beta$ -Secretase Cleavage of $\beta$ -Amyloid Precursor Protein in the Endoplasmic Reticulum/Intermediate Compartment of NT2N Cells, <i>Journal of Cell Biology</i> , 138: 671-680 (August 11, 1997).	
du	107	Diedrich, et al., Nucleotide sequence of a cDNA encoding mouse cathepsin D, Nucleic Acids Research, 18:7184 (1990).	
W	65	Elan Corporation, plc and Pharmacia Corporation announce research collaboration, News 08/09/2000, www.elancorp.com.	
M	66	Evin, et al., Alzheimer's disease amyloid precursor protein (βAPP): proteolytic processing, secretases and βA4 amyloid production, <i>Amyloid; Int. J. Exp. Clin. Invest.</i> 1: 263-280 (September 8, 1994).	
M	67	Haass, et al., Amyloid β-peptide is Produced by Cultured Cells During Normal Metabolism, <i>Nature</i> , 359: 322-325 (September 24, 1992).	
dw	68	Haass, et al., The Swedish Mutation Causes Early-Onset Alzheimer's Disease by β-Secretase Cleavage Within the Secretory Pathway, <i>Nature Medicine</i> , 12: 1291-1296 (December 1995).	
M	69	Haass, et al., β-Amyloid Peptide and 3-kDa Fragment are Derived by Distinct Cellular Mechanisms, <i>Journal of Biochemistry</i> , 268: 3021-3024 (February 15, 1993).	
M	70	Hirosawa, et al., Characterization of cDNA Clones Selected by the GeneMark Analysis from Size-Fractionated cDNA Libraries From Human Brain, <i>DNA Res.</i> , 6(5): 329-336 (October 29, 1999).	

Examiner Date Date	
Signature // // // Considered /2/20/04	

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<sup>&</sup>lt;sup>1</sup> Applicant's unique citation designation number (optional). <sup>2</sup> Applicant is to place a check mark here if English language Translation is attached.

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Complete if Known Substitute for form 1449B/PTO 09/724,569 Applicati n Number INFORMATION DISCLOSURE November 28, 2000 **Filing Date** STATEMENT BY APPLICANT John P. Anderson **First Named Inventor** 2002 **Art Unit** 1632 (use as many sheets as necessary) **Examiner Name** Unknown TECH CENTER 1600/2900 Attomey Docket Number 015270-006446US Sheet of 6

		OTHER PRIOR ART - NON PATENT LITERATURE DOCUMENTS	
Examiner Initials *	Cite No.1	Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc.), date, page(s), volume-issue number(s), publisher, city and/or country where published.	T²
W	71	Hussain, et al., Identification of a Novel Aspartic Protease (Asp 2) as $\beta$ -Secretase, Molecular and Cellular Neuroscience, 14: 419-427 (1999).	
M	72	Kang, et al., The Precursor of Alzheimer's Disease Amyloid A4 Protein Resembles a Cell-Surface Receptor, <i>Nature</i> , 325: 733-736 (February 19, 1987).	
W	73	Kitaguchi, et al., Novel Precursor of Alzheimer's Disease Amyloid Protein Shows Protease Inhibitory Activity, <i>Nature</i> , 331: 530-532 (February 11, 1988).	
M	74	Knops, et al., Cell-type and Amyloid Precursor Protein-type Specific Inhibition of Aß Release by Bafilomycin A1, a Selective Inhibitor of Vacuolar ATPases, Journal of Biological Chemistry, 270: 2419-2422 (February 10, 1995).	
W	75	Koo and Squazzo, Evidence that Production and Release of Amyloid $\beta$ -Protein Involves the Endocytic Pathway, <i>Journal of Biological Chemistry</i> , 269: 17386-17389 (July 1, 1994).	
W	108	Majer, et al., Structure-based subsite specificity mapping of human cathepsin Dusing statine-based inhibitors, <i>Protein Science</i> , 6:1458-1466 (1997).	
M	76	Mullan, et al., A Pathogenic Mutation for Probable Alzheimer's Disease in the APP Gene at the N-Terminus of $\beta$ -Amyloid, <i>Nature Genetics</i> 1: 345-347, (August 1992).	
M	77	PCT Search report for PCT/US99/20881	
dw	78	PCT Search report for PCT/US00/03819	
JW	79	Ponte, et al., A New A4 Amyloid mRNA Contains a Domain Homologous to Serine Proteinase Inhibitors, <i>Nature</i> , 331: 525-527 (February 11, 1988).	
W	109	Saftig, et al., Amyloidogenic Processing of Human Amyloid Precursor Protein in Hippocampal Neurons Devoid of Cathepsin D, <i>Journal of Biological Chemistry</i> , 271:27241-27244 (1996).	
JW	110	Schechter, et al., On the size of the active site in proteases. I. Papain, Biochemical and Biophysical Research Communications, 27:157-162 (1967).	

Examiner Signature	Melide	Date Considered	12/20/04

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<sup>&</sup>lt;sup>1</sup> Applicant's unique citation designation number (optional). <sup>2</sup> Applicant is to place a check mark here if English language Translation is attached.

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Substitute for form 1449B/PTO Complete if Kn wn **Application Number** 09/724,569 INFORMATION DISCLOSURE Filing Dat November 28, 2000 STATEMENT BY APPLICANT John P. Anderson **First Named Inventor** DEC 1 1 2002 Art Unit 1632 (use as many sheets as necessary) **Examiner Name** Unknown ECH CENTER 1600/2900 015270-006446US Attorney Docket Number Sheet

		OTHER PRIOR ART NON PATENT LITERATURE DOCUMENTS	_
Examiner Initials *	Cite No.1	Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc.), date, page(s), volume-issue number(s), publisher, city and/or country where published.	T²
drw	80	Seubert, et al. Secretion of $\beta$ -amyloid Precursor Protein Cleaved at the Amino Terminus of the $\beta$ -amyloid Peptide, <i>Nature</i> , 361: 260-263 (January 21, 1993).	
dul	81	Sinha, et al., Purification and Cloning of Amyloid Precursor Protein $\beta$ -Secretase from Human Brain, <i>Nature</i> , 402: 537-540 (December, 2 1999).	
del	82	Szecsi, The Aspartic Proteases, Scand. J. Clin. Lab. Invest., 52 (suppl. 210): 5-22 (1992).	
W	83	Tanzi, et al., Protease Inhibitor Domain Encoded by an Amyloid Protein Precursor mRNA Associated with Alzheimer's Disease, <i>Nature</i> , 331: 528-530 (February 11, 1988).	
M	93	Thompson, et al., Expression and characterization of human $\beta$ -secretase candidates metalloendopeptidase MP78 and cathepsin D in $\beta$ APP-overexpressing cells, <i>Molecular Brain Research</i> , 48:206-214.	
In	84	Vasser, et al., β-secretase Cleavage of Alzheimer's Amyloid Precursor Protein by the Transmembrane Aspartic Protease BACE, Science, 286 (5440): 735-41 (October 22, 1999).	
dw	.85	Yan, et al., Membrane-anchored Aspartyl Protease with Alzheimer's Disease $\beta$ -Secretase Activity, <i>Nature</i> , 402: 533-537 (December 2, 1999).	
M	101	Young, et al., HIV-1 Protease Inhibitors Based on Hydroxyethylene Dipeptide Isosteres: An Investigation into the Role of the P <sub>1</sub> -Side Chain on Structure-Activity, <i>J. Med. Chem.</i> , 35:1702-1709 (1992).	
dw	86	Zhao, et al., β-Secretase Processing of the β-Amyloid Precursor Protein in Transgenic Mice Is Efficient in Neurons but Inefficient in Astrocytes, Journal of Biological Chemistry, 271: 31407-31411 (December 6, 1996).	

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